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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

PARAS JR, PETER

ART UNIT

PAPER NUMBER

1632

127

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/084,621

Applicant(s)

CHU ET AL.

Examiner

Peter Paras, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 May 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,5-9,11-26,40-49 and 60-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-9,11-26,40-49 and 60-63 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 May 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

Applicant's amendment received on 5/29/03 has been entered. Claims 3-4, 10, 17, 26-39, 50-59 and 64-66 have been cancelled. Claims 1-2, 5-9, 11, 13-16 and 18-24 have been amended. Claims 1-2, 5-9, 11-26, 40-49 and 60-63 are pending and are under current consideration.

#### ***Drawings***

The drawings filed on 5/29/03 are approved.

#### ***Specification***

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 19 of the specification. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The previous rejection of claims 1-2 and 9 under 35 U.S.C. 101 is withdrawn in view of applicant's amendments to the claims.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5-9, 11-25, 40-49, and 60-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose genome comprises a homozygous disruption of the endogenous GPX1 gene and a homozygous disruption of the endogenous GPX2 gene, and wherein said mouse exhibits a phenotype of ileitis, colitis, decreased rate of weight gain, hypothermia, perianal ulceration, diarrhea, wasting syndrome, inflammatory bowel disease, dysplasia in the small bowel, and tumors in the small bowel, does not reasonably provide enablement for the other transgenic mice encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Aspects of the previous rejection are maintained for the reasons of record advanced on pages 3-7 of the Office action mailed on 1/29/03.

Applicant's arguments filed on 5/29/03 have been fully considered but are not found persuasive. Applicants assert that the claimed transgenic mice are enabled to a broader phenotype of cancer rather than the enabled scope as presented by the Examiner. In support of their assertions, Applicants argue that the exemplified transgenic mice develop tumors, which are an indication of cancer. See pages 10-11 of the amendment.

In response, the Examiner maintains that the phenotype arising from disruption of a transgene in a transgenic mouse is unpredictable because phenotypes other than the expected phenotypes may result from said disruption. See Moreadith and Moens on pages 6-7 of the Office action mailed on 1/29/03. The Examiner further maintains that the observed phenotypes, indicated as enabled above, exhibited by the transgenic mice of the claimed invention are observable only as a result of a homozygous disruption of the endogenous GPX I and GPX 2 genes. In particular, the claims are overly broad as they encompass a phenotype of cancer. There are many forms of cancer that affect different tissues and have very different symptoms. The evidence of record while not supporting the breadth of the claims directed to a cancer phenotype, has suggested that the claimed transgenic mice develop tumors in the small intestine. See pages 28-29 of the specification. It appears that the evidence of record may be suggestive of a phenotype of cancer of the small intestine at best.

With regard to claim 40, Applicants argue that the recited phenotype of decreased GPX-I and GPX-GI production is a phenotype that differs from a wild-type phenotype.

In response, the Examiner asserts that decreased GPX-I and GPX-GI production is not an acceptable phenotype, as the double homozygous knockout mice exemplified by the evidence of record do not produce any GPX-I or GPX-GI. Moreover, the enabled phenotypes as recited by the Examiner result from lack of production of GPX-I and GPX-GI, not decreased production of GPX-I and GPX-GI. It would appear that decreased production of GPX-I and GPX-GI does not correlate to any observable

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phenotype exhibited by the claimed transgenic mice. Finally, the evidence of record has not provided guidance as to the degree of a decrease in production of GPX-I and GPX-GI that results in a phenotype, other than no production. It is maintained that a skilled artisan would not know use a transgenic mouse without a phenotype in view of the lack of guidance presented by the evidence of record to that end. See page 7 of the Office action mailed on 1/29/03.

Applicants have argued that claims 60-63 provide mice that are valuable models for studying the functional redundancy of GPX-I and GPX-GI in various tissues.

In response, the Examiner asserts that while the transgenic mice of the invention may be useful for studying functional redundancy, the claims still do not recite a phenotype exhibited by the claimed mice. It is maintained that a skilled artisan would not know use a transgenic mouse without a phenotype in view of the lack of guidance presented by the evidence of record to that end. Moreover, with regard to claim 60 the evidence of record does not support any phenotype exhibited by a transgenic mouse whose genome comprises a homozygous knockout of the Gpx1 gene and a heterozygous knockout of the Gpx2 gene (also see claim 62, for similar deficiencies). See above.

In addition, the aspect of the previous rejection directed to availability of ES cells, as set forth in pages 4-5 of the previous Office action, is maintained over claims 61 and 63 as claims are directed to an animal model. Although the claims also recite that the animal model comprises a transgenic mouse of claim 60, such a recitation is not sufficient to overcome the previous rejection because of the breadth of the term "animal"

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in conjunction with the open claim language, comprising. It appears that the claims may embrace animals other than mice.

### **Conclusion**

**No claim is allowed.**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

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**PETER PARAS**  
**PATENT EXAMINER**

A handwritten signature in cursive script that reads "Pete Paras".